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Acetic Acid Based Dressings on *Pseudomonas aeruginosa* Infected Diabetic Ulcers: A Randomized Controlled Study

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Abstract

Wound infections had increased the risk of amputations in Diabetic patients by 90 times. *Pseudomonas aeruginosa*, has been a local deterrant to wound healing by its various properties of biofilm formation, increased virulence and multi drug resistance by various methods. Unfortunately, due to its resistance to first generation spectrum of antibiotics, and its gradual increase in resistance to third generation cephalosporins, aminoglycosides etc, the need for alternative methodologies arise. Acetic acid helps in local control of the microbe by reducing the wound pH to acidic. This was an Open labelled prospective randomized control trial. Totally 80 patients with diabetic foot ulcers with culture proven *Pseudomonas aeruginosa* positive status were included, and non diabetic ulcers were excluded. Two groups based on simple randomization into test and control groups each containing 40 patients. The control group received traditional saline dressings. The test variables and the control variables were tabulated and compared using Chi square test. The efficacy of 3% Acetic acid in eradication of *Pseudomonas aeruginosa* infected diabetic ulcers was assessed. $p<0.01$ was considered to be statistically significant. At the end of the study, it was seen that there was complete eradication of *Pseudomonas aeruginosa* in 87.5% of the individuals in the test group and 62.5% of the individuals in the control group which was statistically significant ($p = 0.009$). Thus, in conclusion, Acetic-acid based dressings are effective for management of diabetic foot.

Keywords: Acetic acid; Pseudomonas; Dressing.

Introduction

Diabetes mellitus is a disorder characterized by uncontrolled sugar levels in the blood and its various manifestations to the human body. Diabetic foot and diabetic foot ulcers occurs as a complication of its sequelae. Foster et al discovered in 1997 that nearly 30 percent of patients with diabetes mellitus have increased risk of developing foot ulcers. 15% of diabetics developing foot ulcers, accounting for 30% of the hospital admissions with the hospital stay of those patients being 60% longer than the rest of the patients. These high risk patients had an increased risk of amputations[1]. The overall healing period of the diabetic ulcer was estimated to be 3 months with persistence of a small ulcer for more than a year[2]. Various management methodologies have been implemented in treating diabetic wounds including Debridement, Dressings, Infection control, Amputation, correcting vasculopathies, Off-loading. Wound infection deters the healing process of the diabetic ulcer and leads to amputations. It was seen wound infections had increased the risk of amputations by 90 times to that of a non-infected wound[4]. It has been seen that the following microbial organisms are more

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common in diabetic foot ulcer isolates; *S. aureus, E.coli, Pseudomonas, Klebsiella, Citrobacter sp., Proteus sp.* With an overall predominance of *Pseudomonas* and *Staphyloccus aureus.* Biofilm production was seen in almost all organisms associated causing increased virulence and delayed wound healing[4]. *Pseudomonas aeruginosa* is one of the leading nosocomial pathogens worldwide. It is a gram negative microbe[10]. This micro-organism has natural resistance to most structurally unrelated antimicrobials available as studied by Mesaros et al. in 2007, attributing to the low permeability of its outer membrane (1/100 to that of *Escheria coli,* (Livermore, 1984)). The mechanism of resistance in *Pseudomonas aeruginosa* can be attributed to the following mechanisms namely Impermeability, Active efflux, Target modification, Non-enzymatic methods. Various strains of *Pseudomonas aeruginosa* with varied natural has been found to have resistance to the following antibiotics namely *Beta lactams – penicillin G, Aminopenicillins, Antibiotics* combined with beta lactam inhibitors, First, second and third generation cephalosporins, Aminoglycosides. The microbe also acquires additional resistance mechanisms via metallo-beta-lactamase (MBL)-mediated resistance which shows resistance to carbapenems[13]. Infection with micro-organisms usually causes an increase in the virulence factors and taxis of neutrophils towards organisms. In *Pseudomonas aeruginosa* infected ulcers, the organism produces a biofilm which, during taxis of neutrophils releases a series of toxic components. These toxic substances deter phagocytosis and causes oxidative stress which delays the physiological process of wound healing[3]. It is also seen that in chronic wounds, *Pseudomonas aeruginosa* infected wounds having a biofilm will deter the wound healing by increasing the inflammatory response. Acetic acid is considered an antimicrobial agent and has low toxicity[6,7]. It has the following actions[8]. Its acidic nature, ability to Neutralize electrochemical potential, Lowering pH of the wound on application. Thomas bjornsholt *et al.* have evaluated the efficacy of acetic acid in various concentrations and its role in lowering the pH of the wound. It has been seen that the unaltered acetic acid molecule is responsible for lowering the pH and its effect in removing the biofilm also helps in reducing the infective rate of the organism[14]. Kapil *et al.* (2017) have assessed the efficacy of 1% acetic acid in various concentrations towards various microbes and have seen that the local pH of the wound was altered and acetic acid is efficient in eradication of multiple organism and fungi[11]. The effect of low pH on wound healing was also studied by Basavaraj *et al.* (2015). It was seen that the acidic environment also promotes epithelization and angiogenesis. In a histopathological study on chronic wound infections, use of citric acid was shown to enhance epithelization and found to actuate the wound healing process by boosting fibroblastic growth and neovascularization, which increases microcirculation of wounds that enables the formation of healthy granulation tissue, thereby leading to faster healing of wounds[12]. Presence of an infectious component prevents wound healing by various factors. When the contamination increases to a point of critical colonisation or infection, then the infection or the bioburden in the wound becomes a major contributing factor that impedes wound healing[5]. Acetic acid, as seen from above, is bactericidal against many organisms, especially towards *Pseudomonas aeruginosa*. It can be used in concentrations from 0.5–5% as topical applicant in wounds infected with *Pseudomonas aeruginosa* and has been seen to be effective in its eradication. It does not cause removal of epithelialization from 8th day and has no effect in tensile strength of the wound[9]. Use of acetic acid in the concentrations mentioned above can provide a viable alternative to conventional antibiotics in elimination of the organism and thereby help in wound healing, decrease in morbidity and attaining locoregional control. *Pseudomonas aeruginosa*, has been a local deterrant to wound healing by its various properties of biofilm formation, increased virulence and multi drug resistance by various methods. Unfortunately, due to its resistance to first generation spectrum of antibiotics, and its gradual increase in resistance to higher spectrum of antibiotics (third generation *cephalosporins, aminoglycosides*), the need for alternative methodologies arise. It has been shown that the local pH (alkaline) is essential for the ideal growth of the organism. Acetic acid being a weak acid has been used as a time old ingredient which helps in local control of the microbe by its various attributes, one of those including reducing the wound pH to acidic.This study will compare the efficacy of acetic acid based dressings and conventional dressings on *Pseudomonas aeruginosa* infected diabetic ulcers.

Materials and Methods

This was an Open labelled prospective randomized control trial with an aim toanalyse the effect of 3% acetic acid dressings in eradication of *Pseudomonas aeruginosa* in comparison to conventional saline dressings in *Pseudomonas aeruginosa* infected diabetic ulcers. Totally 80 patients including

In-patients and out patients from departments of General Surgery, General Medicine, Cardiology, Nephrology and Neurology from November 2016 to November 2018, were selected. All patients with diabetic foot ulcers with culture proven *Pseudomonas aeruginosa* positive status were included in the study, and those with Ischaemic ulcer, venous ulcer, ulcer with vasculitis, ulcers with osteomyelitic changes, ulcers with bones or tendons exposed and Immunocompromised patients were excluded from the study. Written informed consents were obtained from the patients and detailed clinical history of the patient were collected from the patients who participated in this study. The following details were collected. Name, age, sex, diabetic status, onset and duration of ulcer and culture sensitivity reports on day 0 and day 10. Each patient was followed up for 10 days and their culture reports were analysed. The patients were divided into two groups based on simple randomization into test and control groups each containing 40 patients. 3% acetic acid was prepared by titrating 100% Glacial acetic acid with distilled water. The test group received 3% acetic acid dressing. 3% acetic acid was taken in a sterile container and sterile gauze was soaked in it. After thorough cleansing of the wound with saline, 3% acetic acid is placed over the wound and gamgee pad was placed over it following which the wound was closed in roller bandage. This was done twice daily for 10 days and culture sensitivity was sent on 10th day. The control group received traditional saline dressings. Under aseptic precautions, patient's wound was thoroughly cleansed with saline and sterile gauze was placed over the raw area following which gamgee pad was placed and wound dressed. This was done twice daily for 10 days and culture sensitivity was sent on 10th day.The data was collected and tabulated in an EXCEL spreadsheet. The test variables and the control variables were tabulated and compared using Chi square test. Percentages, mean values and statistical significance values were derived. A type I error of 0.05 was taken into consideration in all analysis. The efficacy of 3% Acetic acid in eradication of *Pseudomonas aeruginosa* infected diabetic ulcers was assessed by reviewing the culture reports on day 10 amongst all patients in both groups using the above statistical tools. $p < 0.01$ was seen and was considered to bestatistically significant in the above study, thereby demonstrating a better outcome in eradication of P. aeruginosa in P. aeruginosa infected diabetic ulcers using 3% acetic acid.

Results and Discussion

It is well known that diabetic ulcers increase the morbidity of the affected individual and delayed wound healing in the presence of infected wounds. It should therefore be mandatory to prevent the development of diabetic foot ulcers at the earliest by identifying diabetic peripheral neuropathic changes. In case of a formed ulcer, in diabetic individuals, adequate care must be initiated to prevent the ulcer from causing irreparable damage. Care involved is multifactorial from the choice of dressings, frequency of dressings, glycaemic control, infection control to debridements. In patients with *Pseudomonas aeruginosa* infected diabetic foot ulcers, due to the prevalence of multiple strains with resistance to betalactams and carbapenems and the ability to produce biofilms, care administered gets difficult due to poor loco-regional control. Acetic acid provides a cheaper alternative in eliminating *Pseudomonas aeruginosa* in *P. aeruginosa* infected diabetic wounds by reducing the pH of the wound and its ability to denature proteins. Literatures reviewed on the use of acetic acid on elimination of *Pseudomonas aeruginosa* in diabetic ulcers and chronic ulcers have shown promising results.Thomas *et al.*, have studied the effect of biofilm formation and antibiotic resistance by *Pseudomonas aeruginosa* and its effect in delayed wound healing. It was seen that biofilms resist and or tolerate all antibiotics and promote pathogen growth. Nagoba *et al.* in 2008 studied the effect of 3–5% acetic acid's topical application two to twelve times over the P. aeruginosa infected diabetic wound successfully eradicated the organism. Ryssel H *et al.* in 2010 studied the effect of acetic acid matrix dressing in burn wounds and found them to be effective in eradication of the organism. In this study, we compared the eradication of *Pseudomonas aeruginosa* in infected diabetic ulcers by using 3% acetic acid to that of conventional saline dressings at the end of 10 days (Fig. 1).

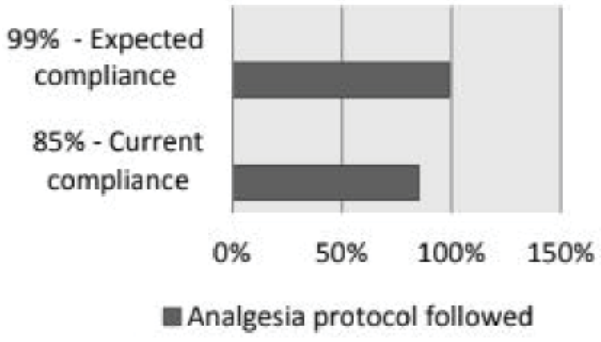

Fig. 1:

All patients received conventional antibiotics via oral and/or parenteral based on culture sensitivity. At the end of the study, both groups of 40 individuals each were compared. It was seen that there was complete eradication of *Pseudomonas aeruginosa* in 35 individuals in those treated with 3% acetic acid to that of 25 individuals in the control group (treated with traditional saline dressings). 70% of the individuals were males in the test group to that of 65% in control group, with the maximum affected individuals in 51–70 age group. 87.5% of the individuals in the test group had complete eradication of the organism with acetic acid dressings and 62.5% of the individuals in the control group had complete eradication of the organism with traditional saline dressings. The percentage elimination of *Pseudomonas aeruginosa* showed a statistical significance ($p = 0.009$), with independent t analysis having ($p = -0.596$) suggesting no bias. It was thus concluded that Acetic acid dressings help in maintaining locoregional control of *Pseudomonas aeruginosa* and eradication of the organism. It is also to be noted that acetic acid proves to be a considerable economic advantage due to its easy availability and better efficacy in eradicating the organism. The limitations of this study to note is its small sample size.

Conclusion

Thus, in conclusion, Acetic-acid based dressings are effective for management of diabetic foot. Acetic acid dressings, in 3% concentrations, help in complete eradication of *P. aeruginosa* in diabetic ulcers. The main advantage being, Acetic acid is easily available and is an economic alternative in providing loco regional control for multidrug resistant Pseudomonas infected diabetic foot ulcers.

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